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Appl. No. 10/668,778
Amdt. dated May 4, 2007
Reply to Office Action of January 5, 2007

PATENT**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. - 62. (Cancelled)

63. (Currently amended) A fragment complementation system, said system comprising[:] a first oligopeptide sequence and a second oligopeptide sequence;

wherein said first oligopeptide sequence is a fusion protein comprised of and in the direction of translation, comprising an N-terminal fragment of a Class A β -lactamase protein at least 25 amino acids in length, fused through a first break-point terminus to a first flexible polypeptide linker and covalently bonded through the C-terminus of a first Class A β -lactamase protein break-point to a first interactor domain; and

wherein said a second oligopeptide sequence is a fusion protein comprised of and in the direction of translation, a second interactor domain and a second flexible polypeptide linker fused through a second break-point terminus to comprising a C-terminal fragment of a Class A β -lactamase protein at least 25 amino acids in length; covalently bonded through the N-terminus of a second Class A β -lactamase protein break-point to a second interactor domain,

wherein said first and second Class A β -lactamase protein break-point termini and second Class A β -lactamase protein break-point;

are within 10 amino acids in either direction from a junction between 2 amino acid residues, wherein said 2 amino acid residues are within a solvent exposed loop between elements of secondary structure and,

wherein upon binding of said first interactor domain with said second interactor domain, said N-terminal fragment and said C-terminal fragment functionally reconstitute to form the Class A β -lactamase protein.

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64. (Currently amended) The fragment complementation system of claim 63, wherein said first oligopeptide and said second oligopeptide comprise a signal peptide that translocates said first oligopeptide and said second oligopeptide through the plasma membrane of the host cell in which said first oligopeptide and said second oligopeptide are expressed.

65. (Canceled)

66. (Currently amended) The fragment complementation system of claim 63, wherein said Class A β -lactamase protein comprises amino acids 26 to 288 of the following sequence:

<u>His Pro Glu Thr Leu Val Lys</u>	<u>Val Lys Asp Ala Glu Asp Gln Leu Gly</u>	
<u>26</u>	<u>30</u>	<u>35</u>
		<u>40</u>
<u>Ala Arg Val Gly Tyr Ile Glu</u>	<u>Leu Asp Leu Asn Ser Gly Lys Ile Leu</u>	
	<u>45</u>	<u>50</u>
		<u>55</u>
<u>Glu Ser Phe Arg Pro Glu Glu</u>	<u>Arg Phe Pro Met Met Ser Thr Phe Lys</u>	
<u>60</u>	<u>65</u>	<u>70</u>
<u>Val Leu Leu Cys Gly Ala Val</u>	<u>Leu Ser Arg Ile Asp Ala Gly Gln Glu</u>	
<u>75</u>	<u>80</u>	<u>85</u>
<u>Gln Leu Gly Arg Arg Ile His</u>	<u>Tyr Ser Gln Asn Asp Leu Val Glu Tyr</u>	
<u>90</u>	<u>95</u>	<u>100</u>
		<u>105</u>
<u>Ser Pro Val Thr Glu Lys His</u>	<u>Leu Thr Asp Gly Met Thr Val Arg Glu</u>	
	<u>110</u>	<u>115</u>
		<u>120</u>
<u>Leu Cys Ser Ala Ala Ile Thr</u>	<u>Met Ser Asp Asn Thr Ala Ala Asn Leu</u>	
<u>125</u>	<u>130</u>	<u>135</u>
<u>Leu Leu Thr Thr Ile Gly Gly</u>	<u>Pro Lys Glu Leu Thr Ala Phe Leu His</u>	
<u>140</u>	<u>145</u>	<u>150</u>
<u>Asn Met Gly Asp His Val Thr</u>	<u>Arg Leu Asp Arg Trp Glu Pro Glu Leu</u>	
<u>155</u>	<u>160</u>	<u>165</u>
<u>Asn Glu Ala Ile Pro Asn Asp</u>	<u>Glu Arg Asp Thr Thr Met Pro Val Ala</u>	
<u>170</u>	<u>175</u>	<u>180</u>
		<u>185</u>

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<u>Met Ala Thr Thr Leu Arg Lys</u>	<u>Leu Leu Thr Gly Glu Leu Leu Thr Leu</u>	
190	195	200
<u>Ala Ser Arg Gln Gln Leu Ile Asp Trp Met Glu Ala Asp Lys Val Ala</u>		
205	210	215
<u>Gly Pro Leu Leu Arg Ser Ala</u>	<u>Leu Pro Ala Gly Trp Phe Ile Ala Asp</u>	
220	225	230
<u>Lys Ser Gly Ala Gly Glu Arg</u>	<u>Gly Ser Arg Gly Ile Ile Ala Ala Leu</u>	
235	240	245
<u>Gly Pro Asp Gly Lys Pro Ser Arg Ile Val Val Ile Tyr Thr Thr Gly</u>		
250	255	260
<u>Ser Gln Ala Thr Met Asp Glu Arg Asn Arg Gln Ile Ala Glu Ile Gly</u>		
270	275	280
<u>Ala Ser Leu Ile Lys His Trp</u>		
285		

(SEQ ID NO:2);

wherein said junction is selected from the group consisting of P174 and N175, E197 and L198, K215 and V216, A227 and G228, and G253 and K254.

67. (Cancelled).

68. (Previously Presented) The fragment complementation system of claim 63, wherein said fragment complementation system further comprises a first peptide that enhances the functional reconstitution of said N-terminal fragment and said C-terminal fragment in comparison with the identical system without said first peptide, wherein said first peptide is 3-12 amino acids in length.

69. (Previously Presented) The fragment complementation system of claim 68, wherein said first peptide is 3 amino acids in length.

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70. (Previously Presented) The fragment complementation system of claim 69, wherein said first peptide is covalently bonded to the active site of a thioredoxin protein, wherein the sequence of said first peptide is GRE.

71. (Currently amended) The fragment complementation system of claim 63, wherein

~~said first oligopeptide further comprises a first polypeptide linker that separates the N-terminal fragment of a Class A β -lactamase protein from the first interactor domain, wherein said first polypeptide linker is 3-30 amino acids in length; and~~

~~said second oligopeptide further comprises a second polypeptide linker that separates the C-terminal fragment of a Class A β -lactamase protein from the second interactor domain, wherein said second polypeptide linker is 3-30 amino acids in length.~~

72. (Previously Presented) The fragment complementation system of claim 71, wherein

~~said first oligopeptide further comprises a first complementation enhancement peptide fused between the N-terminal fragment of a Class A β -lactamase protein and the first polypeptide linker; and~~

~~said second oligopeptide further comprises a second complementation enhancement peptide fused between the C-terminal fragment of a Class A β -lactamase protein and the second polypeptide linker~~

73. (Previously Presented) The fragment complementation system of claim 72, wherein

~~the sequence of said first complementation enhancement peptide is selected from the group consisting of HSE, GRE, EKR, and NGR, and~~

~~the sequence of said second complementation enhancement peptide is selected from the group consisting of REQ, QGN, DGR, GRR and GNS.~~

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74. (Previously Presented) The fragment complementation system of claim 73, wherein

if the sequence of said first complementation enhancement peptide is HSE, then the sequence of said second complementation enhancement peptide is REQ;

if the sequence of said first complementation enhancement peptide is NGR, then the sequence of said second complementation enhancement peptide is selected from the group consisting of REQ and GNS;

if the sequence of said first complementation enhancement peptide is GRE, then the sequence of said second complementation enhancement peptide is DGR; and

if the sequence of said first complementation enhancement peptide is EKR, then the sequence of said second complementation enhancement peptide is GRR.